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FILE 'HOME' ENTERED AT 13:50:07 ON 22 MAR 2004

=> file medline caplus scisearch biosis

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FILE 'SCISEARCH' ENTERED AT 13:50:21 ON 22 MAR 2004

FILE 'BIOSIS' ENTERED AT 13:50:21 ON 22 MAR 2004

=> s immunoglobulin(s)protection(s)factor or fcrp
L1 110 IMMUNOGLOBULIN(S) PROTECTION(S) FACTOR OR FCRP

=> s (chimeric or chimera or fusion)(s)(antibody or antibodies or immunoglobulin?)
L2 43808 (CHIMERIC OR CHIMERA OR FUSION)(S)(ANTIBODY OR ANTIBODIES OR IMMUNOGLOBULIN?)

=> s l1(p)l2
L3 9 L1(P) L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 9 DUP REM L3 (0 DUPLICATES REMOVED)

=> d ibib abs 1-9

L4 ANSWER 1 OF 9 SCISEARCH
ACCESSION NUMBER: 2002:613006 SCISEARCH
THE GENUINE ARTICLE: 574VC
TITLE: Immunization with a polyprotein vaccine consisting of the T-cell antigens thiol-specific antioxidant, Leishmania major stress-inducible protein 1, and Leishmania elongation initiation factor protects against leishmaniasis
AUTHOR: Coler R N (Reprint); Skeiky Y A W; Bernards K; Greeson K; Carter D; Cornellison C D; Modabber F; Campos-Neto A; Reed S G
CORPORATE SOURCE: Infect Dis Res Inst, 1124 Columbia St, Suite 600, Seattle, WA 98104 USA (Reprint); Infect Dis Res Inst, Seattle, WA 98104 USA; Corixa Corp, Seattle, WA 98104 USA
COUNTRY OF AUTHOR: USA
SOURCE: INFECTION AND IMMUNITY, (AUG 2002) Vol. 70, No. 8, pp. 4215-4225.

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NEWS 3	SEP 09	CA/CAplus records now contain indexing from 1907 to the present
NEWS 4	DEC 08	INPADOC: Legal Status data reloaded
NEWS 5	SEP 29	DISSABS now available on STN
NEWS 6	OCT 10	PCTFULL: Two new display fields added
NEWS 7	OCT 21	BIOSIS file reloaded and enhanced
NEWS 8	OCT 28	BIOSIS file segment of TOXCENTER reloaded and enhanced
NEWS 9	NOV 24	MSDS-CCOHS file reloaded
NEWS 10	DEC 08	CABA reloaded with left truncation
NEWS 11	DEC 08	IMS file names changed
NEWS 12	DEC 09	Experimental property data collected by CAS now available in REGISTRY
NEWS 13	DEC 09	STN Entry Date available for display in REGISTRY and CA/CAplus
NEWS 14	DEC 17	DGENE: Two new display fields added
NEWS 15	DEC 18	BIOTECHNO no longer updated
NEWS 16	DEC 19	CROPU no longer updated; subscriber discount no longer available
NEWS 17	DEC 22	Additional INPI reactions and pre-1907 documents added to CAS databases
NEWS 18	DEC 22	IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
NEWS 19	DEC 22	ABI-INFORM now available on STN
NEWS 20	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS 21	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS 22	FEB 05	German (DE) application and patent publication number format changes
NEWS 23	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS 24	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS 25	MAR 03	FRANCEPAT now available on STN

NEWS EXPRESS	MARCH 5 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 3 MARCH 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
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Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0019-9567.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 51

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Development of an effective vaccine against Leishmania infection is a priority of tropical disease research. We have recently demonstrated **protection** against Leishmania major in the murine and nonhuman primate models with individual or combinations of purified leishmanial recombinant antigens delivered as plasmid DNA constructs or formulated with recombinant interleukin-12 (IL-12) as adjuvant. In the present study, we immunized BALB/c mice with a recombinant polyprotein comprising a tandem **fusion** of the leishmanial antigens thiol-specific antioxidant, L. major stress-inducible protein 1 (LmST11), and Leishmania elongation initiation **factor** (LeIF) delivered with adjuvants suitable for human use. Aspects of the safety, immunogenicity, and vaccine efficacy of formulations with each individual component, as well as the pollyprotein referred to as Leish-111f, were assessed by using the L. major challenge model with BALB/c mice. No adverse reactions were observed when three subcutaneous injections of the Leish-111f polyprotein formulated with either MPL-squalene (SE) or Ribi 529-SE were given to BALB/c mice. A predominant Th1 immune response characterized by in vitro lymphocyte proliferation, gamma interferon production, and **immunoglobulin** G2A **antibodies** was observed with little, if any, IL-4. Moreover, Leish-111f formulated with MPL-SE conferred immunity to leishmaniasis for at least 3 months. These data demonstrate success at designing and developing a prophylactic leishmaniasis vaccine that proved effective in a preclinical model using multiple leishmanial antigens produced as a single protein delivered with a powerful Th1 adjuvant suitable for human use.

L4 ANSWER 2 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 2002:337829 SCISEARCH
THE GENUINE ARTICLE: 540RR

TITLE: Prime-boost vaccines encoding an intracellular idiotype/GM-CSF fusion protein induce protective cell-mediated immunity in murine pre-B cell leukemia

AUTHOR: Pasquini S (Reprint); Peralta S; Missiaglia E; Carta L; Lemoine N R
CORPORATE SOURCE: Univ London Imperial Coll Sci Technol & Med, Sch Med, Hammersmith Hosp, Imperial Canc Res Fund, Mol Oncol Unit, London W12 0HS, England (Reprint); Wistar Inst Anat & Biol, Philadelphia, PA 19104 USA
COUNTRY OF AUTHOR: England; USA

SOURCE: GENE THERAPY, (APR 2002) Vol. 9, No. 8, pp. 503-510.
Publisher: NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST, LONDON N1 9XW, ENGLAND.
ISSN: 0969-7128.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 33

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Two vaccines against an intracellularly expressed B cell idlotype were assessed for their ability to induce protective immunity in mice against challenge with a pre-B cell leukemia. One vaccine was based on a plasmid expression vector and the other was a recombinant vaccinia virus; both vaccines expressed a polypeptide derived from the complementarity-determining regions (CDR2-CDR3) of the leukemic clone-specific **immunoglobulin** heavy chain (IgH), as a **fusion** product

with mouse granulocyte-macrophage colony-stimulating **factor** (mGM-CSF). Mice inoculated with either vaccine showed significantly higher survival rates than controls after challenge with leukemia cells. However, **protection** from tumor challenge was optimal when the DNA vaccine was used for priming, followed by a booster immunization with the vaccinia virus recombinant. This vaccination protocol induced resistance not only to the first tumor challenge given shortly afterwards, but also to a second challenge given months later. Both CD4+ and CD8+ T cells contributed to **protection** in vaccinated mice. These data suggest that such a vaccine regimen might reduce the incidence of recurrence in patients with minimal residual disease after conventional therapy.

L4 ANSWER 3 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2002:19753 SCISEARCH
THE GENUINE ARTICLE: 504FX
TITLE: Bacterial lipoprotein-based vaccines induce tumor necrosis factor-dependent type 1 protective immunity against Leishmania major
AUTHOR: Cote-Sierra J; Bredan A; Toldos C M; Stijlemans B; Brys L; Cornelis P; Segovia M; de Baetselier P; Revets H (Reprint)
CORPORATE SOURCE: Free Univ Brussels, Flanders Interuniv Inst Biotechnol, Dept Immunol Parasitol & Ultrastruct, Paardenstr 65, B-1640 Rhode St Genese, Belgium (Reprint); Free Univ Brussels, Flanders Interuniv Inst Biotechnol, Dept Immunol Parasitol & Ultrastruct, B-1640 Rhode St Genese, Belgium; Univ Murcia, Fac Med, Dept Genet & Microbiol, Murcia, Spain
COUNTRY OF AUTHOR: Belgium; Spain
SOURCE: INFECTION AND IMMUNITY, (JAN 2002) Vol. 70, No. 1, pp. 240-248.
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0019-9567.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 47
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Immunity against Leishmania major requires rapid induction of a type 1 immune response in which tumor necrosis **factor** alpha (TNF-a) plays an essential role. Hence, vaccination strategies that simulate the protective immune response found in hosts that have recovered from natural infection provide a rational approach to combat leishmaniasis. One method for optimizing the qualitative and quantitative immune responses after vaccination is to use an adjuvant. In this study we demonstrate that the OprI lipoprotein (L-OprI) from Pseudomonas aeruginosa induces a long-term cellular (gamma interferon [IFN-gamma]) and humoral (**immunoglobulin** G2a) type 1 immune response against a truncated 32-kDa version (COOHgp63) of the 63-kDa major cell surface glycoprotein gp63. By contrast, immunization with COOHgp63 either fused to OprI nonlipoprotein or with no adjuvant did not result in the induction of type 1 immune responses. The adjuvanticity of L-OprI is strongly dependent on its capacity to induce TNF-alpha, since generation of type I immune responses is clearly delayed and impaired in TNF-alpha (-/-) mice. Vaccination with L-OprICOOHgp63 **fusion** protein protected BALB/c mice against L. major infection for at least 19 weeks. Vaccinated mice were largely free of lesions or clearly controlled lesion size on termination of the experiment. The control of disease progression in mice vaccinated with L-OprICOOHgp63 was associated with enhancement of antigen-specific IFN-gamma production. These data indicate that bacterial lipoproteins constitute appropriate adjuvants to include in vaccines against diseases in which type 1 immune responses are important for

protection.

L4 ANSWER 4 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2002:529225 SCISEARCH
THE GENUINE ARTICLE: 565MG
TITLE: Molecular cloning, expression and partial characterization of Xksy, Xenopus member of the Sky family of receptor tyrosine kinases
AUTHOR: Kishi Y A; Funakoshi H; Matsumoto K; Nakamura T (Reprint)
CORPORATE SOURCE: Osaka Univ, Grad Sch Med, Course Adv Med, Div Mol Regenerat Med, 2-2 Yamadaoka, Suita, Osaka 5650871, Japan (Reprint); Osaka Univ, Grad Sch Med, Course Adv Med, Div Mol Regenerat Med, Suita, Osaka 5650871, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: GENE, (17 APR 2002) Vol. 288, No. 1-2, pp. 29-40. Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. ISSN: 0378-1119.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 38
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We isolated a cDNA encoding the Xenopus member of Sky/Axl/Mer receptor tyrosine kinase family (referred as Sky family), termed Xksy. The predicted Xksy protein has conserved structural characteristics of the Sky family: an unique extracellular domain of two **immunoglobulin** (Ig)-like repeats, two fibronectin type III (FNIII)-like repeats and an intracellular tyrosine kinase. Homology analysis of Xksy showed the highest identity to mammalian Sky protein. In contrast to the predominant expression of sky mRNA in the adult mammalian nervous system, Northern blot analysis showed ubiquitous expression of a single 5.2-kb Xksy mRNA in tissues of the adult Xenopus. RNase **protection** assays revealed that, during development, Xksy mRNA is expressed from mid neurulation stage. Levels increase through the tadpole stage and become restricted to the head region in embryos by stage 40. Whole-mount in situ hybridization analyses revealed that expression of Xksy is localized to the nervous system of the tadpole stage, including origins of sensory organs and branchial arches. When a **chimeric** receptor (EGFR-Xksy), composed of the extracellular region of epidermal growth **factor** (EGF) receptor and the transmembrane/ intracellular regions of Xksy, was expressed in a doxycycline repressive manner in HEK 293 cells, EGF-stimulus without doxycycline induced tyrosine phosphorylation of the **chimeric** receptor and evoke morphological changes. EGF treatment also induced growth modifications of EGFR-Xksy cells. And doxycycline pre-treatment eliminated these activities. These findings suggest that Xksy may play an important role in growth, differentiation and the accurate migration of cells during embryogenesis and early neural development. (C) 2002 Elsevier Science B.V. All rights reserved.

L4 ANSWER 5 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2000:723483 SCISEARCH
THE GENUINE ARTICLE: 355QE
TITLE: Genetic immunization of BALB/c mice with a plasmid bearing the gene coding for a hybrid merozoite surface protein 1-hepatitis B virus surface protein fusion protects mice against lethal Plasmodium chabaudi chabaudi PC1 infection
AUTHOR: Wunderlich G (Reprint); Moura I C; delPortillo H A
CORPORATE SOURCE: UNIV SAO PAULO, INST CIENCIAS BIOMED 2, AVENIDA PROF LINEU PRESTES 1374, BR-05508900 SAO PAULO, BRAZIL (Reprint)
COUNTRY OF AUTHOR: BRAZIL
SOURCE: INFECTION AND IMMUNITY, (OCT 2000) Vol. 68, No. 10, pp.

5839-5845.
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904.
ISSN: 0019-9567.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 31

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The genetic immunization of rodents with a plasmid coding for a Plasmodium chabaudi merozoite surface protein 1 (C terminus)-hepatitis B virus surface **fusion** protein (pPcMSP1(19)-HBs) provided **protection** of mice against subsequent lethal challenge with P. chabaudi chabaudi PCI-infected red blood cells. The percentage of survivor mice was higher in DNA-immunized mice than in animals immunized with a recombinant rPcMSP1(19)-glutathione S-transferase **fusion** protein administered in Freund adjuvant, In all mice immunized with the pPcMSP1(19)-HBs, a Th1-specific response, including the production of anti-MSP1(19)-specific **immunoglobulins** predominantly of the **immunoglobulin** G2a subtype and reacting almost exclusively against discontinuous epitopes, was elicited. The coinjection of Th1-type cytokine-expressing plasmids (gamma interferon, interleukin-2, and granulocyte-macrophage colony-stimulating **factor**) mostly abolished **protection** and boosting of MSP1(19)-specific **antibodies.** The inclusion of a lymph node-targeting signal did not significantly increase **protection.** These data provide further evidence that MSP1(19)-HBs DNA constructs might be useful as components of a genetic vaccine against the asexual blood stages of Plasmodium.

L4 ANSWER 6 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 97:703252 SCISEARCH
THE GENUINE ARTICLE: XW396

TITLE: Modulation of keratinocyte growth factor receptor expression in human cultured keratinocytes

AUTHOR: Marchese C; Sorice M; DeStefano C; Frati L; Torrisi M R (Reprint)
CORPORATE SOURCE: UNIV ROMA LA SAPIENZA, DIPARTIMENTO SPERIMENTALE & PATOL, VIALE REGINA ELENA 324, I-00161 ROME, ITALY (Reprint); UNIV ROMA LA SAPIENZA, DIPARTIMENTO SPERIMENTALE & PATOL, I-00161 ROME, ITALY; IST NAZL RIC CANC, SEZ BIOTECNOL, ROME, ITALY; OSPED PEDIAT BAMBINO GESU, IRCCS, DIPARTIMENTO CHIRURG PLAST, ROME, ITALY; IST NEUROL MEDITERRANEO NEUROMED, POZZILLI, ITALY
COUNTRY OF AUTHOR: ITALY

SOURCE: CELL GROWTH & DIFFERENTIATION, (SEP 1997) Vol. 8, No. 9, pp. 989-997.
Publisher: AMER ASSOC CANCER RESEARCH, PUBLIC LEDGER BLDG, SUITE 816, 150 S. INDEPENDENCE MALL W., PHILADELPHIA, PA 19106.
ISSN: 1044-9523.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 33

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Keratinocyte growth **factor** (KGF) belongs to the fibroblast growth **factor** (FGF) family, and its activity seems to be restricted to epithelial cells. It elicits its biological effects through binding to the KGF receptor (KGFR), a splicing transcript variant of FGF receptor 2 (FGFR2). The presence of multiple isoforms of FGFR2 and the overlapping specificities of the FGFs with respect to their receptors do

not allow the use of anti-FGFR **antibodies** as specific immunocytochemical tools. Here we used a **chimeric** protein recently obtained by the **fusion** of KGF to the HFc portion of **immunoglobulin** G (La Rochelle et at, J. Cell Biol., 129: 357-366, 1995) to analyze the expression and distribution of KGFRs in human keratinocytes cultured in chemically defined medium and incubated with different Ca2+ concentrations to modulate their differentiation. We observed at both immunofluorescence and electron microscopic levels and by Western blot analysis of proliferation (K6) or differentiation (K1) markers that KGFR expression is up-modulated during keratinocyte• differentiation. Cytofluorimetric and Western blot analysis revealed that exposure to the high Ca2+ differentiation signal resulted in a significant increase in KGFRs. RNase **protection** assay using a KGFR-specific cDNA probe demonstrated that this effect was-correlated with a >4-fold increase in KGFR transcript level. Our results suggest that the expression of KGFR, unlike that of the epidermal growth **factor** receptor, may control the proliferative-differentiative program from basal to suprabasal cells in human skin.

L4 ANSWER 7 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 94:610350 SCISEARCH
THE GENUINE ARTICLE: PH298
TITLE: PASSIVE-IMMUNITY TO YERSINIAE MEDIATED BY ANTI-RECOMBINANT V-ANTIGEN AND PROTEIN A-V-ANTIGEN FUSION PEPTIDE
AUTHOR: MOTIN V L; NAKAJIMA R; SMIRNOV G B; BRUBAKER R R (Reprint)
CORPORATE SOURCE: MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI, 48824 (Reprint); MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI, 48824; NF GAMALEI INST EPIDEMIOL & MICROBIOL, MOSCOW 123098, RUSSIA
COUNTRY OF AUTHOR: USA; RUSSIA
SOURCE: INFECTION AND IMMUNITY, (OCT 1994) Vol. 62, No. 10, pp. 4192-4201.
ISSN: 0019-9567.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 68

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB LcrV (V antigen), a known unstable 37.3-kDa monomeric peptide encoded on the ca. 70-kb Lcr plasmid of Yersinia pestis, Yersinia pseudotuberculosis, and Yersinia enterocolitica, has been implicated as a regulator of the low-calcium response, virulence **factor**, and protective antigen. In this study, lcrV of Y. pestis was cloned into protease-deficient Escherichia coli BL21. The resulting recombinant V antigen underwent marked degradation from the C-terminal end during purification, yielding major peptides of 36, 35, 34, and 32 to 29 kDa. Rabbit gamma globulin raised against this mixture of cleavage products provided significant **protection** against 10 minimum lethal doses of Y. pestis ($P < 0.01$) and Y. pseudotuberculosis ($P < 0.02$). To both stabilize V antigen and facilitate its purification, plasmid pPAV13 was constructed so as to encode a **fusion** of lcrV and the structural gene for protein A (i.e., all but the first 67 N-terminal amino acids of V antigen plus the signal sequence and **immunoglobulin** G-binding domains but not the cell wall-associated region of protein A). The resulting **fusion** peptide, termed PAV, could be purified to homogeneity in one step by **immunoglobulin** G affinity chromatography and was stable thereafter. Rabbit polyclonal gamma globulin directed against PAV provided excellent passive immunity against 10 minimum lethal doses of Y. pestis ($P < 0.005$) and Y. pseudotuberculosis ($P < 0.005$) but was ineffective against Y. enterocolitica. **Protection** failed after absorption with excess PAV, cloned whole V antigen, or a

large (31.5-kDa) truncated derivative of the latter but was retained (P < 0.005) upon similar absorption with a smaller (19.3-kDa) truncated variant, indicating that at least one protective epitope resides internally between amino acids 168 and 275.

L4 ANSWER 8 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 94:761895 SCISEARCH
THE GENUINE ARTICLE: PU361
TITLE: PROTECTIVE EFFECT OF 55-KD BUT NOT 75-KD SOLUBLE TUMOR-NECROSIS-FACTOR RECEPTOR IMMUNOGLOBULIN-G FUSION PROTEINS IN AN ANIMAL-MODEL OF GRAM-NEGATIVE SEPSIS
AUTHOR: EVANS T J; MOYES D; CARPENTER A; MARTIN R; LOETSCHER H; LESSLAUER W; COHEN J (Reprint)
CORPORATE SOURCE: ROYAL POSTGRAD MED SCH, DEPT INFECT DIS & BACTERIOL, DU CANE RD, LONDON W12 0NN, ENGLAND (Reprint); ROYAL POSTGRAD MED SCH, DEPT INFECT DIS & BACTERIOL, LONDON W12 0NN, ENGLAND; F HOFFMANN LA ROCHE & CO LTD, CH-4002 BASEL, SWITZERLAND
COUNTRY OF AUTHOR: ENGLAND; SWITZERLAND
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (01 DEC 1994) Vol. 180, No. 6, pp. 2173-2179.
ISSN: 0022-1007.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 36
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The aim of this study was to compare the ability of both a 55- and 75-kD soluble tumor necrosis **factor** receptor **immunoglobulin** G **fusion** protein (sTNFR-IgG) in protecting against death in a murine model of gram-negative sepsis. Pretreatment with 250 mu g of the p75 construct delayed but did not avert death in this model, reducing peak bioactive TNF-alpha levels after infection from 76.4 ng ml(-1) in control mice to 4.7 ng ml(-1) in the treated group ($p<0.05$: two-sample t test). However, these low levels of bioactive TNF-alpha persisted in the p75 **fusion** protein-treated animals compared with the controls and were sufficient to mediate delayed death. In contrast, pretreatment with 200 mu g of the p55 sTNFR-IgG gave excellent **protection** against death with complete neutralization of circulating TNF. Studies of the binding of TNF-alpha with the soluble TNFR **fusion** proteins showed that the p75 **fusion** construct exchanges bound TNF-alpha about 50-100-fold faster than the p55 **fusion** protein. Thus, although both **fusion** proteins in equilibrium bind TNF-alpha with high affinity, the TNF-alpha p55 **fusion** protein complex is kinetically more stable than the p75 **fusion** construct, which thus acts as a TNF carrier. The persistent release of TNF-alpha from the p75 **fusion** construct limits its therapeutic effect in this model of sepsis.

L4 ANSWER 9 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 91:314899 SCISEARCH
THE GENUINE ARTICLE: FP086
TITLE: A PROTEIN WITH A BINDING-SPECIFICITY SIMILAR TO NF-KAPPA-B BINDS TO A STEROID-DEPENDENT REGULATORY ELEMENT IN THE OVALBUMIN GENE
AUTHOR: SCHWEERS L A; SANDERS M M (Reprint)
CORPORATE SOURCE: UNIV MINNESOTA, DEPT BIOCHEM, MINNEAPOLIS, MN, 55455
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1991) Vol. 266, No. 16, pp. 10490-10497.
DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 47
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The chicken ovalbumin gene is regulated at the level of transcription by four classes of steroid hormones. A steroid-dependent regulatory element (SDRE) found from -900 to -732 is required for this steroid-mediated induction. To define more precisely sequences of the SDRE required for steroidal induction, a series of exonuclease III deletions were made in the 3' end of the SDRE. **Fusion** genes containing the mutant ovalbumin 5'-flanking sequences linked to the chloramphenicol acetyltransferase structural gene (CAT) were transfected into steroid-responsive primary oviduct cells. These functional studies defined a region of the SDRE from -793 to -759 that is essential for induction by steroids. Analysis of protein interactions in this 34-base pair region by copper-phenanthroline footprinting and methylation interference assays defined nucleotides required for protein binding. Footprinting showed **protection** of residues extending from -784 to -765, an area that included nucleotides that, when methylated, interfered with protein binding. In addition, this footprinted region contained 10 nucleotides that were identical to sequences contained in the beta-interferon gene regulatory element. An oligomer synthesized to this region of homology produced two DNA-protein complexes with oviduct nuclear proteins. Although this region of the interferon gene regulatory element binds the transcription **factor** NF-kappa-B, an oligomer from the **immunoglobulin** kappa-light chain gene known to bind NF-kappa-B did not compete with the SDRE oligomer for binding to oviduct nuclear proteins. Surprisingly, this same NF-kappa-B oligomer was able to restore steroid responsiveness to an SDRE mutant, while an oligomer from the **immunoglobulin** heavy chain gene inserted in the same position did not affect induction by steroids. These data suggest that a protein binding to sequences in the SDRE that are similar to an NF-kappa-B-binding site participates in the steroid-mediated increase in transcription of the chicken ovalbumin gene.

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=> d his

     (FILE 'HOME' ENTERED AT 13:50:07 ON 22 MAR 2004)

     FILE 'MEDLINE, CAPLUS, SCISEARCH, BIOSIS' ENTERED AT 13:50:21 ON 22 MAR
     2004
L1          110 S IMMUNOGLOBULIN(S)PROTECTION(S)FACTOR OR FCRP
L2        43808 S (CHIMERIC OR CHIMERA OR FUSION)(S)(ANTIBODY OR ANTIBODIES OR
L3            9 S L1(P)L2
L4            9 DUP REM L3 (0 DUPLICATES REMOVED)

=> s immunoglobulin(w)protection(w)factor or fcrp
L5           17 IMMUNOGLOBULIN(W) PROTECTION(W) FACTOR OR FCRP

=> s l3 and l5
L6            0 L3 AND L5

=> s (chimeric or chimera or fusion)(p)(antibody? or antibodies? or immunoglobulin?)
L7        66310 (CHIMERIC OR CHIMERA OR FUSION)(P)(ANTIBODY? OR ANTIBODIES? OR
                IMMUNOGLOBULIN?)

=> s l7 and l5
L8            0 L7 AND L5

=> s (immunoglobulin?(w)protection?(w)factor?) or fcrp
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L9          17 (IMMUNOGLOBULIN?(W) PROTECTION?(W) FACTOR?) OR FCRP

=> s l9 and l7
L10          0 L9 AND L7

=> file medline caplus scisearch biosis uspatfull pctfull
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                                                   ENTRY    SESSION
FULL ESTIMATED COST                               98.30      98.51

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FILE 'USPATFULL' ENTERED AT 13:55:08 ON 22 MAR 2004
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FILE 'PCTFULL' ENTERED AT 13:55:08 ON 22 MAR 2004
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=> s (immunoglobulin?(w)protection?(w)factor?) or fcrp
L11        147 (IMMUNOGLOBULIN?(W) PROTECTION?(W) FACTOR?) OR FCRP

=> s (chimeric or chimera or fusion)(p)(antibody? or antibodies? or immunoglobulin?)
L12     133192 (CHIMERIC OR CHIMERA OR FUSION)(P)(ANTIBODY? OR ANTIBODIES? OR
               IMMUNOGLOBULIN?)

=> s l11 and l12
L13        126 L11 AND L12

=> dup rem l13
PROCESSING COMPLETED FOR L13
L14         126 DUP REM L13 (0 DUPLICATES REMOVED)

=> s l11(p)l12
L15         76 L11(P) L12

=> dup rem l15
PROCESSING COMPLETED FOR L15
L16          76 DUP REM L15 (0 DUPLICATES REMOVED)

=> s (mutation or deletion or substitution)(s)fc
L17       5052 (MUTATION OR DELETION OR SUBSTITUTION)(S) FC

=> s l16 and l17
L18          9 L16 AND L17

=> d ibib abs 1-9

L18  ANSWER 1 OF 9  USPATFULL on STN
ACCESSION NUMBER:        2003:153626  USPATFULL
TITLE:                   ENHANCING THE CIRCULATING HALF LIFE OF ANTIBODY-BASED
```

FUSION PROTEINS
INVENTOR(S): GILLIES, STEPHEN, CARLISLE, MA, UNITED STATES
LO, KIN-MING, LEXINGTON, MA, UNITED STATES
LAN, YAN, BELMONT, MA, UNITED STATES
WESOLOWSKI, JOHN, WEYMOUTH, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003105294	A1	20030605
APPLICATION INFO.:	US 1999-256156	A1	19990224 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-75887P	19980225 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: TESTA, HURWITZ & THIBEAULT, LLP, HIGH STREET TOWER, 125 HIGH STREET, BOSTON, MA, 02110
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Page(s)
LINE COUNT: 1022
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are methods for the genetic construction and expression of antibody-based fusion proteins with enhanced circulating half-lives. The fusion proteins of the present invention lack the ability to bind to immunoglobulin Fc receptors, either as a consequence of the antibody isotype used for fusion protein construction, or through directed mutagenesis of antibody isotypes that normally bind Fc receptors. The fusion proteins of the present invention may also contain a functional domain capable of binding an immunoglobulin protection receptor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 2 OF 9 USPATFULL on STN
ACCESSION NUMBER: 2003:64303 USPATFULL
TITLE: Expression technology for proteins containing a hybrid isotype antibody moiety
INVENTOR(S): Gillies, Stephen D., Carlisle, MA, UNITED STATES
Way, Jeffrey, Cambridge, MA, UNITED STATES
Lo, King-Ming, Lexington, MA, UNITED STATES
PATENT ASSIGNEE(S): Lexigen Pharmaceuticals Corp., Lexington, MA (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003044423	A1	20030306
APPLICATION INFO.:	US 2002-93958	A1	20020307 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-274096P	20010307 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: TESTA, HURWITZ & THIBEAULT, LLP, HIGH STREET TOWER, 125 HIGH STREET, BOSTON, MA, 02110
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 2288
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are methods and compositions for efficiently expressing antibody fusion proteins. Antibody fusion proteins of the invention include a hybrid antibody moiety containing sequences from more than one type of antibody and/or mutant antibody sequences. Hybrid antibody fusion proteins of the invention may be produced at high levels and may combine functional properties characteristic of different antibody types in addition to functional properties of a non-antibody moiety.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 3 OF 9 USPATFULL on STN
ACCESSION NUMBER: 2002:266428 USPATFULL
TITLE: Enhancing the circulating half-life of antibody-based fusion proteins
INVENTOR(S): Gillies, Stephen D., Carlisle, MA, UNITED STATES
Burger, Christa, Darmstadt, GERMANY, FEDERAL REPUBLIC OF
Lo, Kin-Ming, Lexington, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002147311	A1	20021010
APPLICATION INFO.:	US 2001-780668	A1	20010209 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-181768P	20000211 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: TESTA, HURWITZ & THIBEAULT, LLP, HIGH STREET TOWER, 125 HIGH STREET, BOSTON, MA, 02110
NUMBER OF CLAIMS: 47
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 1491
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are compositions and methods for enhancing the circulating half-life of antibody-based fusion proteins. Disclosed methods and compositions rely on altering the amino acid sequence of the junction region between the antibody moiety and the fused protein moiety in an antibody-based fusion protein. An antibody-based fusion protein with an altered amino acid sequence in the junction region has a greater circulating half-life when administered to a mammal. Disclosed methods and compositions are particularly useful for reducing tumor size and metastasis in a mammal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L18 ANSWER 4 OF 9 PCTFULL COPYRIGHT 2004 Univentio on STN
ACCESSION NUMBER: 2002072605 PCTFULL ED 20020927 EW 200238
TITLE (ENGLISH): EXPRESSION TECHNOLOGY FOR PROTEINS CONTAINING A HYBRID ISOTYPE ANTIBODY MOIETY
TITLE (FRENCH): TECHNIQUE D'EXPRESSION POUR DES PROTEINES CONTENANT UN FRAGMENT D'ANTICORPS ISOTYPE CHIMERIQUE
INVENTOR(S): GILLIES, Stephen, D., 159 Sunset Road, Carlisle, Ma 01741, US;
WAY, Jeffrey, 108 Fayerweather Street, Cambridge, MA 02138, US
PATENT ASSIGNEE(S): LEXIGEN PHARMACEUTICALS CORP., 125 Hartwell Avenue, Lexington, MA 02173, US [US, US]
AGENT: WALLER, Patrick, R., H.$, Testa, Hurwitz & Thibeault,

L.L.P., High Street Tower, 125 High Street, Boston, MA 02110$, US
LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2002072605	A2	20020919

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM
RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2002-US7011 A 20020307
PRIORITY INFO.: US 2001-60/274,096 20010307

ABEN Disclosed are methods and compositions for efficiently expressing antibody fusion proteins. Antibody fusion proteins of the invention include a hybrid antibody moiety containing sequences from more than one type of antibody and/or mutant antibody sequences. Hybrid antibody fusion proteins of the invention may be produced at high levels and may combine functional properties characteristic of different antibody types in addition to functional properties of a non-antibody moiety.

ABFR L'invention concerne des procedes et des compositions permettant d'exprimer efficacement des proteines hybrides d'anticorps. Les proteines hybrides d'anticorps de cette invention comprennent un fragment d'anticorps chimerique contenant des sequences de plus d'un type de sequences d'anticorps et/ou d'anticorps mutants. Les proteines hybrides d'anticorps chimerique de cette invention peuvent etre produites a des niveaux eleves et peuvent combiner des proprietes fonctionnelles caracteristiques de differents types d'anticorps a des proprietes fonctionnelles d'un fragment qui n'est pas d'un anticorps.

L18 ANSWER 5 OF 9 PCTFULL COPYRIGHT 2004 Univentio on STN
ACCESSION NUMBER: 2001058957 PCTFULL ED 20020827
TITLE (ENGLISH): ENHANCING THE CIRCULATING HALF-LIFE OF ANTIBODY-BASED FUSION PROTEINS
TITLE (FRENCH): AMELIORATION DE LA DEMI-VIE CIRCULANTE DE PROTEINES DE FUSION A BASE D'ANTICORPS
INVENTOR(S): GILLIES, Stephen, D.;
BURGER, Christa;
LO, Kin, Ming
PATENT ASSIGNEE(S): LEXIGEN PHARMACEUTICALS CORP.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001058957	A2	20010816

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE

DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG
CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2001-US4455 A 20010209
PRIORITY INFO.: US 2000-60/181,768 20000211
ABEN Disclosed are compositions and methods for enhancing the circulating half-life of antibody-based fusion proteins. Disclosed methods and compositions rely on altering the amino acid sequence of the junction region between the antibody moiety and the fused protein moiety in an antibody-based fusion protein. An antibody-based fusion protein with an altered amino acid sequence in the junction region has a greater circulating half-life when administered to a mammal. Disclosed methods and compositions are particularly useful for reducing tumor size and metastasis in a mammal.
ABFR L'invention concerne des compositions et des methodes permettant d'ameliorer la demi-vie circulante de proteines de fusion a base d'anticorps. Ces methodes et ces compositions consistent a modifier la sequence d'acide amine de la region de jonction entre la fraction d'anticorps et la fraction de proteine fusionnee dans une proteine de fusion a base d'anticorps. Une proteine de fusion a base d'anticorps comportant une sequence d'acide amine modifiee dans sa region de jonction possede une demi-vie circulante plus longue lorsqu'elle administree a un mammifere. Ces methodes et ces compositions sont notamment utiles pour reduire la taille des tumeurs et les metastases chez un mammifere.

L18 ANSWER 6 OF 9 PCTFULL COPYRIGHT 2004 Univentio on STN
ACCESSION NUMBER: 2001021816 PCTFULL ED 20020820
TITLE (ENGLISH): MODULATION OF IgE RECEPTOR CELL SURFACE EXPRESSION
TITLE (FRENCH): PROCEDE DE MODULATION DE L'EXPRESSION DE LA SURFACE D'UNE CELLULE RECEPTRICE DE L'IMMUNOGLOBINE E
INVENTOR(S): KINET, Jean-Pierre;
DONNADIEU, Emmanuel;
JOUVIN, Marie-Helene;
COOKSON, William;
MOFFATT, Miriam, Fleur
PATENT ASSIGNEE(S): ISIS INNOVATION LIMITED;
BETH ISRAEL DEACONESS MEDICAL CENTER, INC.;
KINET, Jean-Pierre;
DONNADIEU, Emmanuel;
JOUVIN, Marie-Helene;
COOKSON, William;
MOFFATT, Miriam, Fleur
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001021816	A1	20010329

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG
CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2000-US25877 A 20000921
PRIORITY INFO.: US 1999-60/154,924 19990921
ABEN The invention relates to methods and related compositions for modulating cell surface expression of the high affinity receptor for immunoglobulin E, the Fc¾RI receptor. The invention also relates to methods and

related compositions for the treatment and/or prevention of conditions mediated by IgE such as allergic conditions.

ABFR

L18 ANSWER 7 OF 9 PCTFULL COPYRIGHT 2004 Univentio on STN
ACCESSION NUMBER: 2000009560 PCTFULL ED 20020515
TITLE (ENGLISH): GENERATION OF MODIFIED MOLECULES WITH INCREASED SERUM HALF-LIVES
TITLE (FRENCH): PRODUCTION DE MOLECULES MODIFIEES AVEC DEMI-VIE SERIQUE PROLONGEE
INVENTOR(S): GALLO, Michael;
JUNGHANS, Richard;
FOORD, Orit
PATENT ASSIGNEE(S): ABGENIX, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2000009560	A2	20000224

DESIGNATED STATES
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 1999-US18777 A 19990817
PRIORITY INFO.: US 1998-60/096,868 19980817

ABEN In accordance with the present invention, there are provided methods for the extension of serum half-lives of proteinaceous molecules, particularly antibody molecules, and compositions of molecules modified in accordance with the methods of the invention. In accordance with a first aspect of the present invention, there is provided a method of modifying the half-life of an antibody through providing an antibody containing an FcRn binding domain or the genes encoding such antibody and physically linking the antibody or the antibody as encoded to a second FcRn binding domain. In accordance with a second aspect of the present invention, there is provided a molecule that contains at least two distinct FcRn binding moieties.

ABFR La presente invention concerne des procedes d'extension des demi-vies seriques de molecules proteiniques, particulierement de molecules d'anticorps, cette invention concernant egalement des compositions de molecules modifiees selon les procedes de l'invention. Un premier aspect de l'invention concerne un procede de modification de la demi-vie d'un anticorps grace a un anticorps comprenant un domaine de liaison FcRn, ou aux genes codant un tel anticorps fixant physiquement cet anticorps ou l'anticorps ainsi code sur un second domaine de liaison FcRn. Un second aspect de l'invention concerne une molecule renfermant au moins deux fractions de liaison FcRn distinctes.

L18 ANSWER 8 OF 9 PCTFULL COPYRIGHT 2004 Univentio on STN
ACCESSION NUMBER: 1999043713 PCTFULL ED 20020515
TITLE (ENGLISH): ENHANCING THE CIRCULATING HALF-LIFE OF ANTIBODY-BASED FUSION PROTEINS
TITLE (FRENCH): AMELIORATION DE LA DEMI-VIE CIRCULANTE DE PROTEINES HYBRIDES A BASE D'ANTICORPS
INVENTOR(S): GILLIES, Stephen, D.;
LO, Kin-Ming;
LAN, Yan;
WESOLOWSKI, John
PATENT ASSIGNEE(S): LEXIGEN PHARMACEUTICALS CORPORATION
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9943713	A1	19990902

DESIGNATED STATES
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 1999-US3966 A 19990224
PRIORITY INFO.: US 1998-60/075,887 19980225
ABEN Disclosed are methods for the genetic construction and expression of antibody-based fusion proteins with enhanced circulating half-lives. The fusion proteins of the present invention lack the ability to bind to immunoglobulin Fc receptors, either as a consequence of the antibody isotype used for fusion protein construction, or through directed mutagenesis of antibody isotypes that normally bind Fc receptors. The fusion proteins of the present invention may also contain a functional domain capable of binding an immunoglobulin protection receptor.
ABFR On decrit des procedes de construction genetique et d'expression de proteines hybrides a base d'anticorps ayant une demi-vie circulante amelioree. Les proteines hybrides de l'invention sont incapables de se lier aux recepteurs pour le fragment Fc des immunoglobulines, soit en consequence de l'utilisation de l'isotype des anticorps pour construire la proteine hybride, soit par mutagenese dirigee des isotypes des anticorps qui se lient normalement aux recepteurs pour le fragment Fc. Les proteines hybrides de l'invention peuvent egalement contenir un domaine fonctionnel capable de lier un recepteur de protection des immunoglobulines.

L18 ANSWER 9 OF 9 PCTFULL COPYRIGHT 2004 Univentio on STN
ACCESSION NUMBER: 1997043316 PCTFULL ED 20020514
TITLE (ENGLISH): PHYSIOLOGICALLY ACTIVE MOLECULES WITH EXTENDED HALF-LIVES AND METHODS OF USING SAME
TITLE (FRENCH): MOLECULES PHYSIOLOGIQUEMENT ACTIVES A DEMI-VIES PROLONGEES ET METHODE D'UTILISATION DE CES DERNIERES
INVENTOR(S): JUNGHANS, Richard, P.
PATENT ASSIGNEE(S): BETH ISRAEL DEACONESS MEDICAL CENTER, INC.
LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 9743316	A1	19971120

DESIGNATED STATES
W: CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1997-US7707 A 19970506
PRIORITY INFO.: US 1996-60/017,249 19960510
US 1997-8/841,815 19970505

ABEN The present invention is drawn to physiologically active molecules which have extended half-lives in the circulatory system of a subject, compositions which include these molecules, methods of producing the molecules, and methods of using the molecules to treat subjects. The half-lives of the physiologically active molecules are extended by modifying their structure such that they are capable of binding to the IgG protection receptor FcRp. By modifying the physiologically active molecules in this manner, the invention takes advantage of the discovery that the FcRp and the FcRn are the same receptor and that modifying physiologically active molecules such that they are capable of binding the IgG protection receptor FcRp allows these molecules to escape lysosomal catabolism and remain in the circulation of a subject for longer periods of time.

ABFR Molecules physiologiquement actives presentant une demi-vie prolongee dans le systeme circulatoire d'un sujet, compositions comprenant ces molecules, methodes de production de ces molecules et methodes d'utilisation de ces molecules a des fins therapeutiques. Les demi-vies de ces molecules physiologiquement actives sont prolongees par une modification de leur structure qui les rend capables de se fixer aux recepteurs FcRp protecteurs de l'IgG. En modifiant de cette maniere les molecules physiologiquement actives, on met a profit la decouverte du fait que le FcRp et le FcRn sont le meme recepteur et que la modification de ces molecules pour leur permettre de se fixer au recepteur de protection FcRp permet a ces molecules d'echapper au catabolisme lysosomal et de rester dans le systeme circulatoire d'un sujet pendant une plus longue duree.

=> d his

(FILE 'HOME' ENTERED AT 13:50:07 ON 22 MAR 2004)

FILE 'MEDLINE, CAPLUS, SCISEARCH, BIOSIS' ENTERED AT 13:50:21 ON 22 MAR 2004

L1 110 S IMMUNOGLOBULIN(S)PROTECTION(S)FACTOR OR FCRP
L2 43808 S (CHIMERIC OR CHIMERA OR FUSION)(S)(ANTIBODY OR ANTIBODIES OR
L3 9 S L1(P)L2
L4 9 DUP REM L3 (0 DUPLICATES REMOVED)
L5 17 S IMMUNOGLOBULIN(W)PROTECTION(W)FACTOR OR FCRP
L6 0 S L3 AND L5

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L7        66310 S (CHIMERIC OR CHIMERA OR FUSION)(P)(ANTIBODY? OR ANTIBODIES? O
L8            0 S L7 AND L5
L9           17 S (IMMUNOGLOBULIN?(W)PROTECTION?(W)FACTOR?) OR FCRP
L10           0 S L9 AND L7

     FILE 'MEDLINE, CAPLUS, SCISEARCH, BIOSIS, USPATFULL, PCTFULL' ENTERED AT
     13:55:08 ON 22 MAR 2004
L11         147 S (IMMUNOGLOBULIN?(W)PROTECTION?(W)FACTOR?) OR FCRP
L12      133192 S (CHIMERIC OR CHIMERA OR FUSION)(P)(ANTIBODY? OR ANTIBODIES? O
L13         126 S L11 AND L12
L14         126 DUP REM L13 (0 DUPLICATES REMOVED)
L15          76 S L11(P)L12
L16          76 DUP REM L15 (0 DUPLICATES REMOVED)
L17        5052 S (MUTATION OR DELETION OR SUBSTITUTION)(S)FC
L18           9 S L16 AND L17

=>

---Logging off of STN---


=>
Executing the logoff script...


=> LOG Y

COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              44.51     143.02

STN INTERNATIONAL LOGOFF AT 13:58:29 ON 22 MAR 2004
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